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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/533,950 | 05/04/2005 | Andre Roget | 271326US0PCT | 9633 |

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| EXAMINER | |
|---|---|
| HAQ, SHAFIQUL | |
| ART UNIT | PAPER NUMBER |
| 1641 | |

DATE MAILED: 12/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/533,950 | ROGET ET AL. | |
| | Examiner | Art Unit | |
| | Shafiqul Haq | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Information Disclosure Statement*

1. Foreign patent document (FR 2,750,136) cited in IDS has not been considered because a copy of English translation was not provided.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. Claim 1 recites the term "pyrrole polymer" in line 2 for attaching a protein to a conductive support, but the chemical nature and structure of the "pyrrole polymer " (i.e. nature and bond between monomer units as well as the nature of bond formation between active polymer with protein) is unclear.
5. Claim 1 is unclear and indefinite for the term "less than" in lines 11-13. The term "less than" is not defined in the specification and the term "less than" do not indicate the baseline. 0.01 nm thickness is less than 10nm and it is unclear whether this thickness is encompassed by the term "less than 10nm".
6. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: activation step for coupling of proteins with pyrrole.

7. With respect to claim 6, it is not clear what proteins are encompassed by the term "two proteins". Are the "two protein" same or different protein?
8. Claim 8 provides for the use of method of claim 1 for producing a monosensor, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
9. Claim 9 provides for the use of method of claim 1 for producing a biochip, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-3 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Guedon et al (Anal Chem. 2000).

Livache et al disclose a method of immobilization of biological material (e.g. DNA or peptide) to a conductive support (e.g biochip) by means of a pyrrole polymer (see abstract and introduction). The method comprises coupling biomolecules to pyrrole monomer and mixing solutions of pyrrole monomer and biomolecules bearing a pyrrole group (DNA or peptide) to obtain an electropolymerization solution and elctropolymerization to obtain a film of copolymer on conductive medium (see sections 2.1. and 2.3. of page 630). The pyrrole copolymerization process allows the preparation of addressed polypyrrole-DNA/protein on blocks of biosensor array (see section 3.; fig.5 and lines 6-9, right lane of page 633). Examples of immobilization of proteins (e.g ACTH hormone) and DNA (Fig. 5; Fig.6 and section 3.4.) are also disclosed.

Livache et al disclose different thickness (from 2 to 80 nm approximately) which were obtained by applying an amount of current from 10 to 400uC/mm$^2$ (section 3.2., 3.4. and Fig. 4) but do not suggest electopolymerization being carried out with a charge of less that 50uC/mm$^2$, for a synthesis time of less than 1000ms to obtain a film of copolymer thickness to about 10nm.

Guedon et al in a polypyrrole-based DNA sensor disclose six different thickness of polypyrroly-ODN spots made by performing the synthesis for 250ms to 1000ms leading to 9-14 nm thick films (page 6007, left column, left column, lines 3-12). The film synthesis is very fast taking about 500ms to spot an 11 nm thick film by a 2-V electrochemical pulse (page 6004, lines 30-31 of left column and page 6005, left column, lines 7-8). Goedon also discloses that for optimal hybridization signal,

optimal thickness of the spot was found to be close to 11 nm (see abstract; page 6007, lines 1-1-26 of left column and Fig. 6).

Therefore, given the above fact that a film of pyrrole containing copolymer having a thickness close to 11 nm is desirable for optimal hybridization signal (Guedon et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to introduce polymer film thickness close to 11nm (i.e 10nm) in the method of Livache et al, with the expectation of enhancing detection signal and to produce a thickness close to nm within 250ms to 1000ms (Goedon) with a electrode of 50um x 50um, an electric current of less that 50uC/$mm^2$ is obvious as described above.

12. Claims 1-3 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Analytical Biochemistry 1998) in view of Livache et al (Biosensors and Bioelectronics 1998) and Guedon et al (Anal Chem. 2000).

Livache et al (Analytical Biochemistry) disclose a method of immobilization of oligonucleotide (ODN) to a conductive support (e.g DNA chip) electrochemically by means of a pyrrole polymer (see abstract and lines 6-10 of right column of page 188). The method comprises coupling oligonucleotide to pyrrole monomer and mixing solutions of pyrrole monomer and oligonucleotide bearing a pyrrole group to obtain an electropolymerization solution and elctrooxidization to obtain a film of copolymer on conductive medium (Lines 6-10 of right column of page 188 and Fig.1 of page 189). The pyrrole copolymerization process allows the preparation of

addressed ODN-pyrrole on blocks of biosensor array so that different oligonucleotides can be immobilized to different blocks of biochip (see B of Fig.1).

Livache et al disclose (Analytical Biochemistry) different thickness of polypyrrole film deposited on the surface (page 192). Synthesis of the film is stopped when the current applied reaches 125, 160, 200, 250 and 375 nC, values which correspond to respectively- for electrodes measuring 50um x 50um – to 50, 64, 80, 100 and 150 $uC/mm^2$ and to a thickness of 10, 16, 20 and 30 nm.

Livache et al (Analytical Biochemistry) do not disclose coupling proteins to pyrrole monomer but suggest copolymerization of many biological molecules (which includes DNA, proteins etc) for immobilization by means of pyrrole polymerization (lines 42-44 of left column of page 194). Livache et al (Analytical Biochemistry) do not suggest electopolymerization being carried out with a charge of less that $50uC/mm^2$, for a synthesis time of less than 1000ms to obtain a film of copolymer thickness to about 10nm, although a range of thickness and a range of currents applied are disclosed.

Livache et al (Biosensors and Bioelectronics 1998) as described in above paragraph 11 disclose of immobilization of peptide to a conductive support by means of a pyrrole polymer wherein protein is coupled to pyrrole monomer.

Guedon et al in a polypyrrole-based DNA sensor disclose six different thickness of polypyrroly-ODN spots made by performing the synthesis for 250ms to 1000ms leading to 9-14 nm thick films (page 6007, left column, left column, lines 3-12). The film synthesis is very fast taking about 500ms to spot an 11 nm thick film by a 2-V

electrochemical pulse (page 6004, lines 30-31 of left column and page 6005, left column, lines 7-8). Goedon also discloses that for optimal hybridization signal, optimal thickness of the spot was found to be close to 11 nm (see abstract; page 6007, lines 1-1-26 of left column and Fig. 6).

Therefore, given the above fact that a film of pyrrole containing copolymer having a thickness close to 11 nm is desirable for optimal hybridization signal (Guedon et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to include proteins for immobilization as taught by Livache et al (Biosensors and Bioelectronics 1998) and introduce polymer film thickness close to 11nm (i.e 10nm) (as suggested by Guedon et al) in the method of Livache et al (Analytical Biochemistry), with the expectation of enhancing detection signal and to produce a thickness close to 11nm (i.e. 10nm) within 250ms to 1000ms (Goedon) with a electrode of 50um x 50um, an electric current of less that 50uC/mm$^2$ is obvious as described above.

13. Claims 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) and Guedon et al (Anal Chem. 2000) as applied to claims 1-3 and 6-9 above, and further in view of Caillat et al (US 6,803,228).

Livache et al and Guedon et al disclose a method of immobilization of biological material (e.g. DNA or peptide) to a conductive support (e.g biochip) by means of a pyrrole polymer as describes above in paragraph 11 but the references fail to disclose pyrrole functionalized with succinimide or maleimide for coupling to protein.

Caillat et al disclose pyrrole polymer functionalized with N-hydroxysuccinimide and maleimide for coupling to biomolecules (see 3rd compound from top in column 4 and lines 63-67).

Therefore, given the fact that functionalization of pyrrole with N-hydroxysuccinimide or maleimide is know and common in the art (Caillat et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to functionalize pyrrole monomer with N-hydroxysuccinimide or maleimide in the method of Livache et al, with the expectation of producing similarly useful conductive support containg polymer of pyrrole coupled with protein.

14. Claims 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998), Guedon et al (Anal Chem. 2000) and Caillat et al (US 6,803,228) as applied to claim 4 in the preceding paragraph, and further in view of Bianchi et al (US 2003/0207400 A1).

Above paragraph 13, describe a method of immobilization of biological material (e.g. DNA or peptide) to a conductive support (e.g biochip) by means of a pyrrole polymer and also disclose pyrrole functionalized with succinimide or maleimide for coupling to protein but the references do not disclose the linkers use to functionalize pyrrole with maleimide as claimed in claim 5.

Bianchi et al disclose different linkers (see scheme 15, 20 and 28) to functionize pyrrole with thiol, maleimide or amino groups and the linkers are either the same as or homologs of the linkers of the instant claim 5.

Therefore, given the fact that functionalization of pyrrole with N-hydroxysuccinimide or maleimide is know and common in the art (Caillat et al) and linkers of different chain length can be employed (Banchi et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to functionalize pyrrole monomer with N-hydroxysuccinimide or maleimide using the linker of Banchi et al, in the method of Livache et al, with the expectation of producing similarly useful conductive support containg polymer of pyrrole coupled with protein.

***Conclusion***

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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